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Seasonal, Geographic, and Temporal Trends of *emm* Clusters Associated With Invasive Group A Streptococcal Infections in US Multistate Surveillance

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To the Editor

Previous reports have demonstrated that 90% of invasive group A *Streptococcus* (GAS) strains in the United States represent approximately 25 different *emm* types, with most disease occurring in winter and early spring [1–3]. However, little is published about more complex geographical and temporal trends for these infections. An *emm*-cluster system that classifies the numerous GAS *emm* types [4] into 48 functional *emm* clusters sharing structural and binding properties has been established [5]. This clustering scheme complements an *emm* patterning system devised 20 years ago, which associates specific markers within *emm* and neighboring related genes with tissue tropisms exhibited by GAS strains [6]. The *emm* clusters are useful in predicting basic genetic features of GAS isolates because they are markers that correlate with M protein functions and antigens as well as the genetic determinants of other features such extracellular matrix binding proteins [5, 7–9]. The *emm* cluster typing is easy to use, and cluster type can be predicted from *emm* typing results [4, 5, 10].

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We report *emm* clusters associated with invasive GAS infections in surveillance areas in 9 US states from 1 January 2003 through 31 December 2013, identified through the Centers for Disease Control and Prevention (CDC)'s Active Bacterial Core surveillance (ABCs), and evaluate overall and state-specific seasonal and temporal distribution of *emm* clusters.

During 11 years of surveillance, we identified 114 different *emm* types among 10 175 isolates causing invasive GAS disease. An *emm* cluster was attributed to 10 136 (99.6%) isolates, with a total of 24 different *emm* clusters represented. Almost all (99.8%) of the cluster-associated isolates belonged to 11 *emm* clusters (in decreasing order of frequency: E4, AC3, E3, AC4, E6, AC5, E1, E2, D4, M6, M5).

When analyzing the proportions of *emm* clusters over time, we observed that isolates belonging to AC clusters (AC3, AC4, and AC5) peaked in winter (January to March) while those belonging to E clusters (E1, E2, E3, E4, and E6) were the most common during summer (Figure 1). During winter, AC cluster and E cluster isolates were associated with a similar average number of invasive GAS infections (147 and 145, respectively), with each accounting for 45% of all infections. In contrast, during summer, E cluster isolates were associated with an average of 100 infections (66% of all infections), compared with an average of 39 infections (25% of all infections) for AC cluster isolates.

The *emm* cluster D4 represented up to 10% of invasive GAS infections in overall ABCs data from 2004 to 2008 but dropped to around 1% in the following years (Figure 1). We observed different peak periods for D4 infections in ABCs surveillance areas across the states (eg, Colorado peaked in 2004–2005, Oregon in 2005–2006, New Mexico in 2007–2008; data not shown). Similarly, other predominant *emm* clusters (eg, M5, M6, E6) peaked in different states at different times, which is compatible with a possible link between introduction of specific *emm* type and/or *emm* cluster in a community and subsequent local population immunity over time.

These data suggest that isolates from prevalent AC and E clusters may possess different capacity for transmission or infection during the summer, but the reason for this difference is unknown and may extend beyond the *emm* gene to additional surface proteins such as M-like proteins and other adhesins. Immunity induced by *emm* types belonging to the same *emm* cluster should be analyzed in more detail.

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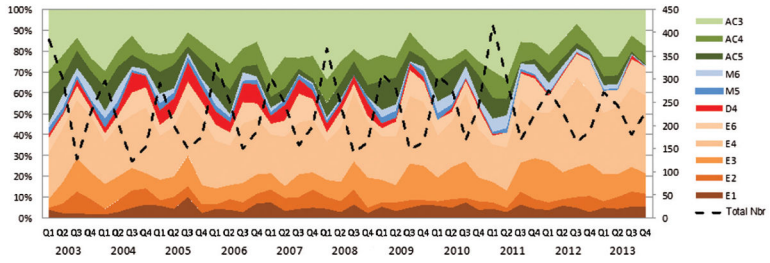

Figure 1.

Distributions of *emm* clusters associated with invasive group A *Streptococcus* (GAS) infection in Active Bacterial Core surveillance (ABCs), 2003–2013. The horizontal axis represents time (quarter and year). The left vertical axis represents the proportion of invasive GAS infections associated with the 11 most frequently identified *emm* clusters in the ABCs, using a color code. The right vertical axis represents the absolute total number of invasive GAS infections reported to ABCs, as shown by the black dashed line.